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| Application of: | Ensoli | Confirmation No.: | 9400 |
| Application No.: | 09/555,534 | Art Unit: | 1648 |
| Filed: | May 31, 2000 | Examiner: | Stucker, Jeffrey J. |
| For: | HIV TAT, OR DERIVATIVES THEREOF FOR PROPHYLACTIC AND THERAPEUTIC VACCINATION | Attorney Docket No.: | 11340-003-999 (formerly 204.610) |

**DECLARATION OF SHAYNE GAD, Ph.D. UNDER 37 C.F.R. § 1.132**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, SHAYNE GAD, Ph.D., do declare as follows:

1. I have over 28 years experience as a toxicologist and consultant in the research and development of products in, *inter alia*, the biotechnology and pharmaceutical industries. I have a Ph.D. in pharmacology and toxicology from University of Texas at Austin and am a Diplomat of American Board of Toxicology (D.A.B.T.) and a fellow of the Academy of Toxicological Sciences (A.T.S.). I am currently principal of Gad Consulting Services, in which capacity I assist clients in evaluating the safety of biotechnology and pharmaceutical products, obtaining regulatory approval and with respect to other compliance issues before a number of United States and foreign regulatory bodies. My education and experience are summarized on my Curriculum Vitae, which is attached hereto as Exhibit 1.

2. I have been asked to evaluate whether the compositions of HIV-1 Tat protein ("Tat") produced according to the purification methods described by Chang *et al.*, 1997, AIDS 11:1421-1431 ("the Chang reference;" attached hereto as Exhibit 2) would be suitable for administration to a human. In my opinion, the phrase "suitable for administration to a human" means that the composition is sufficiently safe for administration to human patients using the criteria for safety defined by regulatory agencies such as the Food and Drug

Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA). As discussed in detail herein and for the reasons set forth below, it is my judgment and opinion that the Tat compositions resulting from the two purification methods described on page 1424 of the Chang reference would not be suitable for administration to a human.

First Chang Reference Tat Purification Method

3. I first address the composition produced by the method described on page 1424 of the Chang reference under the heading "Tat protein and anti-Tat antibody." The Chang reference states that the procedure involves expression of the protein in *E. coli* and then isolation of Tat through rounds of high-pressure liquid chromatography (HPLC) and ion-exchange chromatography, which the Chang reference indicates is performed as described in two earlier references, reference 18, which is Ensoli *et al.*, 1993, J. Virology 67: 277-287 (attached as Exhibit 3), and reference 44, which is Bohan *et al.*, 1992, Gene Expression 2:391-407 (attached as Exhibit 4). The relevant passage of Ensoli *et al.*, reference 18, is on page 278, column 1. The relevant passage of Bohan *et al.*, reference 44, is in the paragraph spanning pages 393 to 395, which indicates that the HPLC is reverse phase HPLC. The Tat is then lyophilized and, prior to use, resuspended in a buffer of PBS containing 0.1% Bovine Serum Albumin (BSA) and 0.1 mM dithiothreitol (DTT). In the procedures involving use of Tat reported in the Chang reference, plasticware was rinsed in either PBS-BSA buffer or 10% Fetal Calf Serum (FCS)-RPMI.

4. I am informed that a solvent commonly used for reverse phase HPLC is acetonitrile, usually also containing trifluoroacetic acid (TFA). I am also informed that the HPLC step would not be performed on the *E. coli* extract but, rather, would follow the ion-exchange chromatography in the purification protocol. Thus, assuming use of a solvent containing acetonitrile and TFA, and based upon the foregoing understanding regarding order of the steps, one would expect acetonitrile and TFA to contaminate the resulting Tat composition. Acetonitrile and TFA would be considered in process impurities.

5. Acetonitrile and TFA are each very toxic both acutely and upon repeat exposure and both are mutagens (*see, e.g.*, Ahmed *et al.*, 1992, Pharmacol. Toxicol. 70:322-330, attached as Exhibit 5; Robles *et al.*, 2005, Acetonitrile, in *Encyclopedia of Toxicology, Second Edition*, (Wexler, ed.) Elsevier, Philadelphia, PA, pp. 28-30, attached as Exhibit 6; Toxsys database Record No. AL7700000 for Acetonitrile, attached as Exhibit 7; and Toxsys database Record No. AJ9625000 for Acetic acid, trifluoro, attached as Exhibit 8). Levels of

acetonitrile in therapeutics are very restricted. TFA is not recognized as an allowed pharmaceutical ingredient in any form. In addition, since TFA is a mutagen and a teratogen, it would be strenuously avoided in the production process of any therapeutic. As such, these solvents should be avoided in any production process for a therapeutic and would not be used in any production process where they might appear as a detectable impurity. Accordingly, compositions of Tat purified using acetonitrile and TFA as solvents would not be suitable for administration to a human.

Second Chang Reference Tat Purification Method

6. Second, I have also considered the method for purifying Tat described in the Chang reference on page 1424 in the paragraph spanning the two columns under the heading "Purification of recombinant Tat protein by heparin affinity chromatography." In this method, *E. coli* cells expressing Tat were sonicated in lysis buffer and the resulting lysate clarified by centrifugation, the supernatant was incubated with heparin-Sepharose prewashed with lysis buffer, and the supernatant was fractionated by heparin-Sepharose chromatography, washing the column with lysis buffer, and eluting the Tat from the column with the same lysis buffer containing 2 M NaCl. The column fractions containing the purified Tat are the final product of the purification method and contain the lysis buffer. The passage indicates that the lysis buffer contains 0.2 mM phenylmethylsulfonyl fluoride (PMSF). Since the final step of the purification contains the 0.2 mM PMSF, it is not just a process impurity, but a component of the Tat composition.

7. PMSF, like acetonitrile and TFA, is very toxic (*see, e.g.*, Gomez-Cambronero *et al.*, 1989, In. Arch. Allergy Appl. Immunol. 4:362-368, attached as Exhibit 9; Lotti *et al.*, 1991, Toxicol. Appl. Pharmacol. 108:234-241, attached as Exhibit 10; and Massicotte *et al.*, 1999, Neurotoxicology 20:749-759, attached as Exhibit 11). PMSF is not allowed as a pharmaceutical ingredient of any form and would not even be allowed in any process where it could be detected as an impurity. Since, in this second purification method disclosed by the Chang reference, PMSF is an actual component of the Tat composition, this composition would not be a composition suitable for administration to humans.

Conclusion

8. In conclusion, based upon the presence of acetonitrile and TFA as process impurities in the composition resulting from the first purification method of the Chang

reference, assuming the use of a solvent containing acetonitrile and TFA, and the presence of PMSF as a component of the composition resulting from the second purification method of the Chang reference, I conclude that neither method results in a Tat composition that would be suitable for administration to a human.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that I make these statements with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, and any patent issuing thereon.

Date: December 13, 2005

Shayne Gad, Ph.D.

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## QUALIFICATIONS SUMMARY

Over 28 years experience as a toxicologist, statistical consultant, manager and consultant on research and development in the chemical, consumer product, contract testing, biotechnology, medical device, and pharmaceutical industries. Experienced in occupational and industrial toxicology, development programs (both preclinical and clinical) and study design, conduct and reporting;, in evaluating clinical and product safety data, in training and managing staff; in dealing with a wide range of U.S. and foreign regulatory bodies, commercial concerns, and contract research organizations; in labeling and other FDA compliance issues for drugs, devices and dietary supplements; identifying, developing and putting into everyday use new technology; in writing reports, position papers, Material Safety Data Sheets, MAA/PLA/IND/NDA/PNA toxicology and pharmacokinetic summaries and package inserts; in preparing INDs, NADAs , IDEs and 510(k)s; in preparing labels and package inserts for drugs, devices and consumer products; in presentations to FDA and in designing experiments, designing and executing surveys; in the pharmacokinetic and statistical analysis of both experimental and clinical data; in risk assessment; in Proposition 65 assessments and labeling; in the registration of OTC, dietary supplement, nutraceutical, and sterilant products with FDA; in providing litigation support, and in the production and development of biologic products.

## PROFESSIONAL POSITIONS

**Principal,** Gad Consulting Services, 1994-present
**President,** Incara/Aeolus Pharmaceuticals, April 2004 to present
**Director of Toxicology,** Synergen, 1993 - 1994
**Director of Medical Affairs Product Support Services**, Becton Dickinson, 1991-1993
**Senior Director of Product Safety and Metabolism**, G.D. Searle, 1989 - 1991
**Director of Toxicology**, G.D. Searle, 1986-1989
**Manager, Mammalian Toxicology**, Allied Corporation, 1980-1986
**Supervisor of Inhalation and Neurotoxicology**, Shell Research, 1979-1980
**Fellow/Group Leader for Inhalation and Neurotox**, Chemical Hygiene Fellowship, 1977-1979

## EDUCATION

Ph.D., Pharmacology/Toxicology, University of Texas at Austin, 1977.

B.S., Chemistry and Biology (two majors), Whittier College, 1970.

**KEY ACCOMPLISHMENTS**

- Directed the design, conduct, writing and successful filing of 65 complete INDs plus 2 PLA, 2 MAA, 4 NADA and 10 NDA safety packages on antiinfectives, antivirals, vaccines, cardiovascular, gastrointestinal, anti-inflammatory, central nervous system, and immune modulatory products derived from both biotechnology and traditional synthetic organic processes for US and foreign filings. Also 32-510(k)s and 3 PMAs plus OTC petitions and sterilant approvals for medical devices.

- Developed and implemented programs to clarify and solve problems/issues around the preclinical, clinical, and manufacturing safety of pharmaceutical products and medical devices, keeping development, production and marketing of drugs on or near plan.

- Oversaw completion, identified and solved quality problems, and completed reports on clinical trials. Designed minority subject recruitment plans for NIH intramural studies.

- Product project team member for eight potential drug products through the course of preclinical and clinical development. Provided safety oversight and counsel for clinical development of drugs and devices.

- Directed positive regulatory interactions with domestic and foreign regulatory agencies, allowing product approval/registration, and initiation and continuation of clinical trials.

- Performed risk assessments and prepared reports on them for pharmaceutical, industrial, agricultural and environmental agents.

- Created and directed programs to provide highly interactive safety assessment support to drug discovery groups, allowing more rapid, efficient and effective identifications of lead compounds and product candidates.

- Reviewed and provided recommendations on 102 potential in-license packages. Key member of small negotiating team for five foreign and domestic compounds.

- As study director, responsible for the design, conduct and reporting of over 900 studies of all types: primate, canine, acute, subchronic, chronic, carcinogenicity, reproductive and developmental toxicity, inhalation, neurotoxicity, immunotoxicity, in vitro toxicity, and environmental toxicity.

- Directed the conduct of over 9000 device safety assessment studies a year, upgraded all laboratory operations and changed the focus of a 20- person group from a contract testing lab to a full range, product support organization. Prepared group to successfully complete their first FDA GLP inspection in 10 years.

- Initiated and managed occupational toxicology program at Searle, identifying needs, developing data and generating Material Safety Data Sheets for all compounds and process intermediates, making them available world-wide by an electronic system. Generated airborne control objectives for all production materials, allowing cost effective engineering of safe facilities, compliance with domestic and international regulations, and flexible management of synthesis and manufacturing operations.

- Initiated and directed the development of a computerized indexing and retrieval system of thirty years of data on biocompatibility and safety of medical devices and their components and constituent materials.

- Developed, validated, put into use and got acceptance of new test methods and techniques (functional observational battery [FOB]; mouse ear swelling test [MEST]; in vitro screens for hepatotoxicity and cardiotoxicity; reduced animal use designs) which are faster, more effective, and use fewer animals and less test compound. The FOB is the starting point for EPA's and FDA's neurotoxicity evaluations. The MEST is now accepted by international regulatory agencies.

## PROFESSIONAL SOCIETIES AND HONORS

Diplomat of American Board of Toxicology (1981-present)
Fellow, Academy of Toxicological Sciences (1999-present)
Society of Toxicologic Pathologists (2002-present)
Society of Toxicology (SOT)
Nominations Committee (elected) - 1992
Placement Committee- 1985-88, 1997-2000
Reproductive & Developmental Specialty Section - Newsletter editor, 1984-1994
Occupational Tox Specialty Section -Vice President 1997-1998; President 1999-2000
Regulatory Toxicology Section – Vice President 1999-2000; President 2000-01
Neurotoxicology section – Chain, Nominating Committee 2003-2004
Animals in Research Committee – 1983-6: Chair 1985-6
American College of Toxicology:
Council 1987-1989
Vice President 1989
President Elect 1990

President 1991
Past President 1992
Roundtable Toxicology Consultants :
President-elect 1997-9
President 1999-2001
Treasurer 2002-2004
Midwest SOT: Council 1987-1989
Vice President 1990
Teratology Society
Biometrics Society
American Statistical Society
*Toxicology Methods* - Editor-in-Chief and founder
*Journal of Fire Science* - editorial board
*Journal of Applied Toxicology* - editorial board
*Inhalation Toxicology* – editorial board
*International Journal of Toxicology* – editorial board
*Toxicology and Industrial Health* - editorial board
*Acute Toxicology* - associate editor
*Toxicology and Applied Pharmacology*, *Fundamental & Applied Toxicology*, *Toxicological Sciences*, *In Vitro Toxicology*, and *Toxicology Letters* – Reviewer
American Council on Science and Health – Board of Scientific and Policy Advisors

**PUBLICATIONS**

29 books
36 independent chapters
102 papers
174 presentation/abstracts

**WORK EXPERIENCE**

April 1994 to present:

GAD CONSULTING SERVICES - *Principal*

Providing regulatory, statistical, preclinical and clinical study support services to over 220 clients in the pharmaceutical, biotechnology, dietary supplement, medical device and animal health industries. The care of the business is supporting pharmaceutical development in the U.S. and internationally with successfully opening 61 IND's in the areas of antiviral, hematologic agents, and products, CNS, oncology, cardiovascular, vaccines, neurology, analgesia and others. Also technical consulting, occupational toxicology, neurotoxicology training and evaluation, statistical analysis and report writing for contract research organizations (both preclinical and clinical). Due diligence of potential products and companies for investors and companies. Expert witness support in pharmaceuticals, medical devices, poisoning, occupational toxicology and for workman's compensation cases.

July 1993 to April 1994:

SYNERGEN - *Director of Toxicology*

Responsible for all aspects of safety assessment of potential drugs being developed by Synergen. Supervised a staff of 4. Wrote safety and pharmacology sections of MAA filing for Antril. Developed compound retention and departmental SOP systems. Oversaw safety assessment and pharmacology for the development of a protein therapeutic for Parkinson's.

June 1991 to July 1993:

BECTON DICKINSON - *Director, Medical Affairs Product Support Services*
Responsible for all aspects of biological safety for Becton Dickinson products. Supervised a staff of 19 with an operating budget of $2.4 MM. Laboratory performed some 9200 biological and analytical chemistry assays annually. Frequent direct interaction with regulatory, quality assurance, product development, division medical directors and marketing.

May 1989 to June 1991:

G.D. SEARLE & CO. - *Senior Director of Product Safety and Metabolism.*
Responsible for all aspects of safety testing for Searle compounds and intermediates. Supervised staff of 49 (11 PhD/DVMs, 10 direct reports), including pathology, histology, hematology and the below detailed toxicology operation, including a $3.44 MM operating budget. Member of Portfolio Management Committee for prioritization of R&D compounds. Frequent direct interaction with foreign firms for licensing, and with both domestic and international regulatory agencies and plants. Developed and put in place worldwide occupational Airborne Control Objectives and Material Safety Data Sheets (MSDS) available on electronic mail system. Responsible for coordination and integration of efforts with Belgian laboratory. Reviewed and approved/released all safety study protocols, reports and IND/NDA summaries. Integrated *in vitro* lab into support of Discovery operations with validated hepatocyte, myocyte, and fibroblast target organ toxicity screens.

May 1986 to May 1989:

G.D. SEARLE & CO. - *Director of Toxicology.*
Responsible for all product safety/toxicity and health effects testing including internal (chronic, subchronic, subacute, reproductive, developmental and genetic toxicity, including primate and canine studies) and external testing programs for development of new and defense of existing products. Also responsible for all MSDS and worker safety support data development. Supervised staff of 34 and directed testing program in support of potential new drugs and existing products, including insuring smooth interface and coordination with Pathology, Metabolism, Analytical, Discovery, Pharmaceutical and Chemical Development, Regulatory, Project Management and Clinical functions. Developed system for integrated (pharmacology/ toxicology/pathology/clinical) planning, interpretation and problem solving down to study basis. Overall project team leader for development of biotechnology derived pharmaceutical products. Initiated and staffed *in vitro* lab to develop library of specific target organ screening tests. Responsible for an operating budget of $1.94 MM plus contract budget. Responsible for preparation of toxicology summaries, and for IND/NDA preparation and submission. Frequent direct interactions with FDA and foreign

regulatory agencies on pre-IND, IND, NDA and post-marketing matters.

May 1980 to May 1986:

ALLIED CORPORATION - *Manager, Mammalian Toxicology.*

Responsible for all mammalian toxicity testing for Allied Corporation, including the operation of the entire Department of Toxicology laboratory (a 17,000 square foot building with a staff of 26) and all external contract testing (including placing and monitoring studies at domestic and foreign laboratories). Recruited and trained staff, equipped and put into operation AALAC certified laboratory. In-house testing included acute, subacute, and subchronic oral, dermal and inhalation studies and specialty reproductive, behavioral, hematological and renal function toxicity studies. Preparation of risk assessments, submissions and presentations to regulatory agencies and trade associations.

September 1979 to May 1980:

SHELL DEVELOPMENT LAB - *Supervisor of Inhalation and Neurotoxicology at Shell Westhollow Center.*

Responsible for bringing on line new inhalation toxicology research facility, (design of air handling control and data acquisition systems, selection and purchasing of equipment, development of techniques and SOPs, and hiring and training of technicians) and for designing and conducting studies at that facility.

August 1977 to September 1979:

UNION CARBIDE TOXICOLOGY LABORATORY - BUSHY RUN RESEARCH CENTER - Chemical Hygiene Fellowship (CHF). *Fellow*

Developed system for assessment of toxicity of polymer thermal decomposition products (developed equipment, protocols and personnel). System certified to test by City of New York for combustion toxicity testing and as such evaluated 50 materials in 1979. Member of NBS ad hoc committee for development of standardized combustion toxicology test protocol. Conceived, developed and implemented initial program (personnel and procedures) for GLP quality assurance at the CHF. Provided statistical consulting expertise to corporation.

*Group Leader for Inhalation and Neurotoxicology.*

Responsible for performance of all inhalation studies at CHF, including 2-year multiple species studies. Supervised one Ph.D. and nine technicians. Included among these studies were specialized inhalation and neurotoxicology studies, including inhalation, behavioral teratology, reproduction and dominant lethal studies for gases, vapors, aerosols and powders. Also brought on-line new testing procedures for guinea pig sensitization.

## MILITARY SERVICE

June 1970 to April 1974 (Active):

Served on riverine craft in Mekong Delta of Vietnam and as O.I.C. of Armory, Quonset Point, Rhode Island. Served on *USS Intrepid* (CVS-11) as special weapons officer, deck division officer and as First Lieutenant. Qualified as O.D. underway on *Intrepid.* Made several deployments overseas - mainly to Europe

and the Mediterranean. Released from active duty in the permanent grade of LT(jg). Received Silver Star, 3 Bronze Stars, 3 Purple Hearts.

July 1974 to December 1994 (Reserves):

Served in a number of billets, including as executive and commanding officer. Mobilized for eight months active duty in Persian Gulf region, 1990-1991. Retired as Captain. Holds current (2003) top secret clearance.

## TRAINING COURSES

Supervisory Management
Management by Objectives
Managerial Accounting
Effective Leadership
Behavioral Toxicology
Chemical Mutagens
Principles and Methods of Detection
Inhalation Toxicology Workshop - Lovelace Institute
Use of Context MBA
HTML
SPSS
SAS
Aerosol Measurement (University of Minnesota)
Basic Project Management (AMA)
Financial Management for Non-Financial Managers
Performance Management System
Operations Research and Analysis (U.S. Navy)
Effective Project Team Operation
WordPerfect
Statgraphics
Excel
Internet
STN (CAS)
WIN/NOLIN

## TRADE ASSOCIATIONS/GOVERNMENT PANELS

Industrial Health Foundation:
- Chromates Committee (1980-1985)
- Chair of Toxicology Subcommittee (1982- 1985)
Nylon 6 Committee (1980-1985)
- Cyclohexanone Committee
- Chairman of Toxicology Subcommittee (1981)

CMA - Ketones Committee (1980-1985)
MMFPA - Toxicology Subcommittee (1980-1981)
NBS- Combustion Toxicology Task Force (1977-1979)
CMA- Phthalate Esters Committee
Special consultant for statistical analysis and risk assessment (1982-1983)
- Lubricant Additives Panel : consultant on sensitization (1999-2003)

CPSC - Consumer Product Safety Commission
Toxicology Advisory Board (1982-1985)
AIHC - Neurotoxicology Subcommittee (1986-1988)
EPA - Science Advisory Board Neurotoxicology Panel(1988)
- Neurotoxicology Risks Assessment Review Panel (1992)

- Neurotoxicity Test Guidelines Panel (1992)

NIH - Occupational Health and Safety Study Section (1989-1993)

- Review panel: Biodefense and SARS Product Development (2004)

NIEHS - Superfund Center Fund grant review panel (1987, 1990, 1991 and 1994 ). Subchair in 1991 and 1994.

IARG - Chair of Organotypic Work Group Eye Irritation Alternatives Group (1993)

DOE -Risk assessment special review panel (1994)

Family Health International/NIH

HIVNET Microbicide and STD Working Group (1997- present)

American Council Science and Health – Koop Select Panel on the Safety of Plastics (1998-9)

Life Sciences Research Office – AIRC Panel (2001-Present)

## PROFESSIONAL SOCIETY/GOVERNMENT APPOINTMENTS

SOT - Animals in Research Committee
(Member 1984-1987; Chairman 1987-1989)
- Placement Committee (1986-1988;1997-present)

CAAT - (Johns Hopkins) - Grants Reviewer, (1985-present)
Panelist, Team for Critical Review of Alternatives to the Rabbit Eye Irritation Test.

ACT - Publicity Committee (1985-present)
- Membership Committee - Chair (1987-1989),
- Animals in Research Committee - Chair (1988-1991)
- Member (1993-present)

NIH, NIEHS, Superfund, Department of Energy, Demeter Fund, and Canadian government - Grant Reviewer

Center for Professional Advancement
- Drug Safety Evaluation (Faculty)
- Safety Assessment of Medical Devices
(Director, New Jersey and Amsterdam courses, 1993, 1994 and 1996, San Francisco course 1998, 2002,
- Safety Testing for Personal Care and Consumer Products
CoDirector, New Jersey and Amsterdam courses, 1999
- Drug and Biologic Safety Evaluation; CoDirector, New Jersey and Amsterdam courses, 1999-2004; Director, New Jersey course, 2000, 2001, 2002, 2003, 2004; San Francisco, 2004; San Diego, 2004

ACSH - Safety of Plastics Blue Ribbon Panel, 1999

## ACADEMIC INVOLVEMENT

Adjunct Professor of Toxicology, Duke University Medical Center

Guest lecturer at University of Kansas, University of Pittsburgh, University of Texas, Rutgers University, Johns Hopkins University, North Carolina State University, Campbell University, and Whittier College

Ph.D. Thesis Committee - Doreen Waldron Lechner; University of Medicine and Dentistry of New Jersey (Newark), 1981-1984.

Ph.D. Thesis Committee - Brian Czerniecki; Rutgers Medical School

(Piscataway), 1985-1987.
Adjunct Associate Professor of Toxicology, College of Saint Elizabeth. Developed B.S. toxicology program, designed and taught toxicology/lecture and laboratory courses and pathology lecture courses (4 lecture and 3 lab courses in a two year cycle).
Board of Trustees, Whittier College (2004-present)

Symposia and Courses Organized, Taught and Chaired:

- An Evaluation of Alternatives to the Draize Eye Test: Special One Day Workshop, Johns Hopkins, April, 1988
- Toxicology as a Career, at ACT Meeting, November, 1986
- Alternatives to Animals in Toxicology, at SOT Meeting, March,1987
- Regulatory Requirements for Safety Testing - A Workshop at Animal Research and Testing: Humane Frontiers: For the Scientific Center for Animal Welfare at Rockefeller University, October, 1987
- Screening for Neurotoxicity, Raleigh, NC, April , 1988
- Statistics for Toxicologists, short course at the ACT Meeting, October, 1988
- Statistics for Toxicologists, short course at the SOT Meeting, February, 1989
- Refinements of Animal Experiments in Toxicology, at the SOT Meeting, February, 1989.
- Biostatistical Analysis of Segment II Studies, symposium at the Teratology Society Meeting, June, 1989
- Toxicology Roundtable, Lake Geneva, WI, September, 1989
- Acute Toxicity: Data Generation, Management and Use, symposium at the ACT Meeting, October, 1989
- Experimental Models in Toxicology, symposium at the ACT Meeting, October, 1989
- 1990 ACT Annual meeting
- Nontraditional Routes in Toxicology, symposium at the ACT Meeting, October 1991
- Safety Reasons for the Withdrawal of Marketed Drugs: Why Did Preclinical Testing Fail?, symposium at the ACT Meeting, October, 1993
- Practical Applications of Toxicokinetics in the Safety Assessment of Drugs and Medical Devices, symposium at the ACT Meeting, November, 1996
- Statistical Analysis and Experimental Design of Carcinogenicity Bioassays, course at ACT Meeting, November, 1997
- Large Animal Toxicology Studies: Design, Conduct and Statistical Analysis, course at ACT Meeting, November, 1998
- Multiple Chemical Sensitivity: The Great Debate, symposium at ACT Meeting, November, 1998
- Experimental Design and Toxicology/Safety Assessment, course taught by special invitation, Center for Veterinary Medicine, Food and Drug Administration, December 8, 1998
- Statistics for Toxicologists, course taught on contract, Canadian regulatory agencies, Ottawa, Canada, January 24-26, 2000.
- Risk Assessment for the GMP Pharmaceutical Manufacturing Industry, Siegfried Chemical, Switzerland, November13-14, 2001
- Are Dietary Supplement Safe as Currently Regulated? The Great Debate,

symposium at ACT meeting, November, 2002.

- Nonclinical Safety Evaluation for Registration of Pharmaceuticals and Biotechnology Products, CIT, Evreux, France, October 2003.
- Statins: Do the benefits outweigh the risks? The Great Debate, symposium at ACT meeting, November, 2003.
- Mold: High risk or hype? The Great Debatre, symposium at ACT meeting, November, 2004.
- Drug Development for Venture Capitalists; 2004 San Diego, San Francisco and Boston.

## PUBLICATIONS

### BOOKS

1. Gad, S.C. and Weil, C.S. *Statistics and Experimental Design for Toxicologists.* Telford Press, Caldwell, NJ, 372 pages (1986).
2. Frazier, J.; Gad, S.C., Goldberg, A.M. and McCaulley, J.; *A Critical Appraisal of Alternatives to the Rabbit Eye Irritation Test.* Mary Ann Liebert, New York, 136 pages (1987).
3. Gad, S.C. (Ed). *Handbook of Product Safety Evaluation.* Marcel Dekker, New York, 638 pages (1988).
4. Gad, S.C. and Chengelis, C.P. *Acute Toxicology: Principles and Methods.* Telford Press, Caldwell, NJ, 530 pages (1988).
5. Gad, S.C. and Weil, C.S. *Statistics and Experimental Design for Toxicologists, 2nd Edition.* Telford Press, Caldwell, NJ, 380 pages (1988).
6. Gad, S.C. *Combustion Toxicology.* CRC Press, Inc., Boca Raton, FL, 202 pages (1990).
7. Gad, S.C. and Chengelis, C.P. (Ed). *Animals Models in Toxicology.* Marcel Dekker, New York. 884 pages (1992).
8. Gad, S.C. *In Vitro Toxicology.* Raven Press, New York. 290 pages (1993).
9. Gad, S.C. and Kapis, M.B. *Non-Animal Techniques in Biomedical and Behavioral Research and Testing.* Lewis Publishers, Ann Arbor, MI. 264 pages (1993).
10. Gad, S.C. *Safety Assessment for Pharmaceuticals.* Van Nostrand Reinhold, New York, (1994).
11. Chengelis, C.P., Gad, S.C. and Holson, J. *Regulatory Toxicology,* Raven Press, New York (1995).
12. Gad, S.C. and Taulbee, S.M. *Handbook of Data Recording, Maintenance and Management for the Biomedical Sciences.* CRC Press, Boca Raton, FL (1996).
13. Gad, S.C. *Safety Evaluation of Medical Devices,* Marcel Dekker, New York (1997)
14. Gad, S.C. and Chengelis, C.P. *Acute Toxicology: Principles and Methods.,* 2nd Ed. Academic Press, San Diego, CA. (1997).
15. Gad, S.C., Hartung, R., Henderson, R.F., Krenzelok, E.P., Mehendale, H.M., Plaa, G.L., Wexler, P., and Witschi, H. *Encyclopedia of Toxicology,* Academic Press, San Diego, CA (1998).
16. Gad, S.C. *Statistics and Experimental Design for Toxicologists,* 3rd Edition, CRC Press, Boca Raton, Fl. (1998).
17. Gad, S.C. (Ed). *Handbook of Product Safety Evaluation.*, 2nd Edition, Marcel Dekker, New York, 638 pages (1999).
18. Gad, S.C. *In Vitro Toxicology.* 2nd Edition, Taylor & Francis, Philadelphia, PA. (2000).
19. Gad, S.C. *Regulatory Toxicology,* 2nd Edition, Taylor & Francis, Philadelphia, PA

(2001).

20. Gad, S.C. *Safety Evaluation of Medical Devices,* 2nd Edition, Marcel Dekker, New York (2001)

21. Gad, S.C. (Ed). *Animals Models in Toxicology,* 2nd Ed., Marcel Dekker, New York. (2003).

22. Gad, S.C. *Drug Safety Evaluation,* John Wiley & Sons, New York (2002).

23. Gad, S.C. *Encyclopedia of Pharmaceutical Development, 9 volumes,* John Wiley & Sons, New York (In preparation).

24. Gad, S.C. *Safety Pharmacology,* CRC Press, Boca Raton, FL. (2003)

25. Gad, S.C. *CROs in Pharmaceutical and Medical Device Development,* Taylor and Francis, Philadelphia (2003))

26. Gad, S.C., Mehendale, H.M., Wexler, P.,and Witschi, H. *Encyclopedia of Toxicology, 2nd Edition,* Academic Press, San Diego, CA (In press).

27. Gad, S.C., *Statistics and Experimental Design for Toxicologists,* 4th Ed., CRC Press, Boca Raton, FL (In press).

28. Gad, S.C., *Target Organ Toxicity*: *The GI Tract*; Taylor & Francis, Philadelphia (In preparation)

29. Gad, S.C. and Brock, W.J., *International Regulatory to Safety Evaluation of Pharmaceuticals and Medical Devices*, CRC Press, (in preparation)

30. Gad, S.C. *Pediatric Toxicology in Pharmaceutical and Medical Device Development.* Human Press (In preparation).

31. Gad, S.C. and Barbare, R.R. *Bayesian Statistics for Clinical and Preclinical Research.* Human Press (In preparation).

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87. Gad, S.C. (2000) Large Animal Species as Models in Toxicology, *Inter. Journal of*

*Toxicology* 19(2):129-132.

88. Gad, S.C. (2000) Pigs and Ferrets as Models in Toxicology and Biological Safety Studies, *Inter. Journal of Toxicology* 19:149-168.

89. Gad, S.C. (2000) Marketing Yourself as an Expert Witness and Consultant in Toxicology, *Comments on Toxicology*, 7:139-170.

90. Gad, S.C. (2002) The Fifth Trienial Toxicology Salary Survey, *International J. Toxicol* 21:323-328.

91. Gad, S.C. (2003) Active Metabolites in Drug Development, *Current Opinions in Pharmacology*, 3:98-100.

92. Gad, S.C. and S.E. (2003), *International Journal of Toxicology*, Are Dietary Supplements Safe as Currently Regulated?, 22:1-8, 2003

93. Gad, S.C. and S.E. (2003), *International Journal of Toxicology*, The Dog Functional Observation Battery (FOB) for use in Pharmaceutical Safety Evaluation Studies, 22:1-8, 2003

94. Gad, S.C. (2004), *Regulatory and Safety Evaluation Newsletter*, Test Materials in Control Animals; Or Be Careful What You Ask, February, 2004.

## PRESENTATIONS

1. Leslie, S.W., Gad, S.C., Brown, R.G., Smith, R.V. Actions of Antioxidants on Isolated Tissue and Subcellular Fraction Preparations, presented at A.P.H.A., November, 1976 Meetings in Orlando, FL.

2. Gad, S.C., and Brown, R.G. Pharmacological Activity in Agents Isolated from the Blue-Green Algae, Oscillatoria Williamsii and Agmenellum Quadruplicatum, presented at AAAS, February, 1978 Meetings in Washington, DC.

3. Gad, S.C., Leslie, S.W., and Acosta, D. Inhibitory Actions of BHT on Isolated Rat and Rabbit Ileum and Atria, presented at ASPET-SOT, August, 1978 Meeting in Houston, TX.

4. Gad, S.C. Design of Inhalation Chambers presented at the Toxicology Roundtable - November, 1978.

5. Gad, S.C., Chin, B.H., McKelvey, J.A., Acosta, D.A., and Leslie, S.W. Cardiovascular Toxicity of BHT and BHA, presented at the SOT 1979 Meetings in New Orleans, LA.

6. Gad, S.C., Maronpot, R.R., McKelvey, J.A., and Turney, R.A. Niax Catalyst ENS-Subchronic Neuropharmacology and Neurotoxicology, presented at the SOT 1979 Meetings in New Orleans, LA.

7. Gad, S.C. Design and Analysis of Dominant Lethal Studies, presented at the Toxicology Roundtable - November 1979.

8. Gad, S.C. NCI Bioassay Statistical Analysis Method, presented at the Toxicology Roundtable, 1979.

9. Rezazedeh, S. Mehdi, Gad, S.C., van Baalen, C. and Brown, R.G. A Pharmacological Study of Agents from Two Blue-Green Algae, presented at The Annual Meeting of Texas

Pharmacologists, May, 1980, Austin, TX.

10. Gad, S.C. A Sensory/Neuromuscular Screen for Use in Industrial Toxicology, presented at the SOT 1981 Meetings in San Diego, CA.

11. Weil, C.S., and Gad, S.C. Statistics in Toxicology Workshop, presented at the ESOT 1981 Meetings in Dublin, Ireland.

12. Gad, S.C. Statistical Analysis of Behavioral Toxicology Data Workshop, presented at the ESOT 1981 Meetings in Dublin, Ireland.

13. Gad, S.C. Statistics for Toxicologists, presented as a part of 1981 Rutgers Seminars in Toxicology Program (October 21, 1981).

14. Gad, S.C. Statistical Decision Trees in Toxicology, presented at the Toxicology Roundtable - October, 1981.

15. Gad, S.C., Gavigan, F.A., Adams, W.D., and Schieman, G. Macrocyclic (Crown) Ethers: Their Toxicity Neuromuscular, Pharmacology and Structure Activity Relationships, presented at the 1982 SOT Meeting in Boston, MA.

16. Derelanko, M.J., Gad, S.C., Powers, W.J., Mulder, S.B., and Gavigan, F.A. Subacute Oral Toxicity of Cyclohexanone Oxime, presented at the 1982 FASEB Meetings.

17. Gad, S.C. Industrial Toxicology, seminar presented at the University of Texas at Austin, November, 1982.

18. Gad, S.C. Alternative Methods for Industrial Toxicology Laboratories, presented at the Toxicology Roundtable - October, 1982.

19. Derelanko, M.J., Gad, S.C., Gavigan, F., Walsh, R.D. and Dunn, B.J. Acute Dermal Toxicity of Dilute Aqueous Hydrofluoric Acid, presented at the 1983 SOT Meeting in Las Vegas, NV.

20. Gad, S.C. , Powers, W.J., Derelanko, M.J., Dunn, B.J., Mulder, S.B., Babich, P.C. Acute, Subacute, and Subchronic Toxicity Studies of Cyclohexanone Oxime, presented at the 1983 SOT Meeting in Las Vegas, NV.

21. Powers, W.J., Gad, S.C., Mulder, S., Brand, K.M., and Hoffman, G. Sex and Strain Differentiation of Subchronic Caprolactam Nephrotoxicity in Rats, presented at the 1983 SOT Meeting in Las Vegas, NV.

22. Kaplan, H.L., Grand, A.F., Switzer, W.G., and Gad, S.C. Acute Inhalation Toxicity of the Smoke Produced by Five Halogenated Polymers, presented at the 1983 SOT Meeting in Las Vegas, NV.

23. Gad, S.C. Toxicity of Cyclohexanone Oxime, seminar presented at New Jersey School of Medicine & Dentistry, February, 1983.

24. Hoffman, G., and Gad, S.C. Isocyanic Acid - Acute Inhalation and Pulmonary Irritation, presented at the Mid-Atlantic SOT Meeting Wilmington, DE in May, 1983.

25. Gad, S.C., Derelanko, M.J., and Gavigan, F. Innovative Designs for Acute Systemic Toxicity Studies, presented at the American College of Toxicology Meeting in Arlington, VA in December, 1983.

26. Gad, S.C., Dunn, B.J., Reilly, C., and Dobbs, D.W. Alternative Test Methods: Development and Validation by an Industrial Laboratory, presented at the American College of Toxicology Meeting in Arlington, VA in December, 1983.

27. Gavigan, F., Derelanko, M.J., Cramp, A.L., and Gad, S.C. Identification of Potential Antidote Candidates for Acute Oral Exposure to Stannous Fluoborate Solution (SF), presented at the American College of Toxicology Meeting in Arlington, VA in December, 1983.

28. Powers, WJ, Gad, SC, Darr, RW and Dunn, BJ. Acute and Subacute Toxicity of Selexol in Mammalian Systems, presented at the Society of Toxicology Meeting in Atlanta, GA in March, 1984.

29. Powers, WJ, Gad, SC, Mulder, SB and Siino, KM. Subacute Comparative Toxicity Study of Lead Sulfate and Lead Dioxide, presented at the 1984 SOT Meeting in Atlanta, GA.

30. Powers, WJ, Gad, SC, Derelanko, MJ and Siino, KM Effects of Therapeutic Agents on Chromium Induced Acute Nephrotoxicity, presented at 1984 SOT Meetings in Atlanta, GA.

31. Gad, S.C., Gavigan, F.A., Siino, K.M., and Reilly, C. The Toxicology of Eleven Ionophores: Neurobehavioral, Membrane and Acute Effects and Their Structure Activity Relationships, presented at the 1984 SOT Meetings in Atlanta, GA.

32. Kaplan, H.L., Switzer, W.G., and Gad, S.C. Comparative Inhalation Toxicity of the Combustion Products of Two Nylons and Douglas Fir, presented at the 1984 SOT Meetings in Atlanta, GA.

33. Derelanko, M.J., Gad, S.C., Dunn, D.J., Gavigan, F., and Walsh, R.D. Toxicity of Diacetylenic Compounds: Structure - Activity Relationships, presented at the 1984 SOT Meetings in Atlanta, GA.

34. Gad, S.C. Innovative and Alternative Designs for Acute Toxicity Studies, presented at the SOT Workshop on Current Practices for Increased Efficiency in the Use of Animals for Research and Testing, Atlanta, GA March, 1984.

35. Gad, S.C. Alternative Methods and Study Designs for Industrial Toxicology Laboratories, presented at Rutgers Toxicology Seminar, April 11, 1984.

36. Gad, S.C. Industrial Toxicology: Principles, Practices and Practical Examples, presented as part of Molecular and Biochemical Toxicology Course, University of Kansas, April 24-26, 1984.

37. Gad, S.C. Toxicology of Cationic Ionophores, presented as graduate seminar at University of Kansas, April 26, 1984.

38. Gad, S.C. Teratology Studies on Caprolactam in the Rat and Rabbit, presented at An Industry Approach To Chemical Risk Assessment in Arlington, VA (May, 1984).

39. Gad, S.C. "Nylon 6 Combustion Toxicity Studies", presented at An Industry Approach To Chemical Risk Assessment in Arlington, VA (May 1984).

40. Cramp, A. L., and Gad, S.C. "Acute Inhalation Toxicity of N-(2,3-eopxpropyl)-phthalimide in the Rat", presented at the 1984 ACT Meeting in Arlington, VA.

41. Gad, S.C., Dunn, B.J., and Dobbs, D.W. "The Mouse Ear Swelling Test as an Alternative Dermal Sensitization Model", presented October 23, 1984 at the John Hospkins In Vitro Toxicology Symposium.

42. Gad, S.C. Alternative Designs For Acute Systemic Toxicity Studies, presented at Mid-Atlantic SOT Symposium in Clifton, NJ in November, 1984.

43. Dunn, B.J., Gad, S.C., and Dobbs, D.W. Development of an Alternative Dermal Sensitization Test: Mouse Ear Swelling Test (MEST), presented at the Mid-Atlantic SOT Fall Symposium, November 9, 1984.

44. Dobbs, D.W., Dunn, B.J., and Gad, S.C. Development and Validation of the Mouse Ear Swelling Test (MEST), presented at the American College of Toxicology Meeting in Arlington, VA, November, 1984.

45. Walsh, R.D., Dunn, B.J., and Gad, S.C. Dermal and Ocular Irritancy of Industrial Chemicals. Correlations and Distribution of Results and Effects of Study Design Alterations, presented at the American College of Toxicology Meeting in Arlington, VA, November, 1984.

46. Gavigan, F.A., Reilly, C., and Gad, S.C. Comparison and Development of Dermal Dosing Techniques in Rats and Rabbits, presented at the American College of Toxicology Meeting in Arlington, VA, November 1984.

47. Siino, K.M., Powers, W.J., and Gad, S.C. Subacute Comparative Absorbance Study of Lead Sulfate and Lead Dioxide, presented at the American College of Toxicology Meeting in Arlington, VA, November, 1984.

48. Steinhoff, D., Gad, S.C., and Hatfield, G.K. Carcinogenicity Study with Sodium Dichromate in Rats, presented at 6th International Cancer Symposium, Vienna, VA, November, 1984.

49. Gad, S.C., Derelanko, M.J., Gavigan, F.A., and Babich, P.C. Evaluation of Acute Hematotoxicity of Hydroxylamine Sulfate by Dermal Routes in Rats and Rabbits, presented at the Society of Toxicology Meetings in San Diego, CA, March, 1985.

50. Gad, S.C., Dunn, B.J., and Dobbs, D. W. Development of the Mouse Ear Swelling Test an Alternative Dermal Sensitization Model, presented at the Society of Toxicology Meetings in San Diego, CA, March, 1985.

51. Dunn, B.J., Gad, S.C., and Dobbs, D.W. Validations of the Mouse Ear Swelling Test (MEST) as an Alternative Dermal Sensitization Model, presented at the Society of Toxicology Meetings in San Diego, CA, March, 1985.

52. Gad, S.C., Darr, R. W., Cramp, A.L., Hoffman, G., and Rusch, G.M. Acute, Subacute and Subchronic Inhalation Toxicity of Hexafluoroisobutylene, presented at the Society of Toxicology Meetings in San Diego, CA, March, 1985.

53. Powers, W.J., Siino, K.M., and Gad, S.C. Inhibition of Chromium-Induced Acute Nephrotoxicity by Ascorbic Acid, presented at the Society of Toxicology Meetings in San Diego, CA March, 1985.

54. Gad, S.C., Walsh, R.D., and Dunn, B.J. Correlation of Dermal and Ocular Irritancy of Industrial Chemicals, Society of Comparative Ophthalmology, April, 1985.

55. Gad, S.C. Statistical Analysis of Preclinical Study Designs in Toxicology, presented at American Statistical Association Biopharmaceutical Workshop, Muncie, In, May, 1985.

56. Gad, S.C. The MEST (Mouse Ear Swelling Test), at LSR Seminars in Toxicology, Suffolk, England, May, 1985.

57. Gad, S.C. Techniques for Management and Career Development of Animal Care Personnel in the Toxicology Laboratory, presented at American Association of Laboratory Animal Science (Delaware Branch) Meeting in Meadowlands, May, 1985.

58. Dunn, B.J., Gad, S.C., and Dobbs, D.W. The Mouse Ear Swelling Test, presented at American Association of Laboratory Animal Science (Delaware Branch) Meeting at the Meadowlands, NY, May, 1985.

59. Gad, S.C. Developing Toxicology Protocols, presented at Johns Hopkins Toxicology '85 Continuing Education Course in Baltimore, June, 1985.

60. Gad, S.C., Dobbs, D.W., Dunn, B.J., Reilly, C., and Walsh, R.D. Elucidation of the Delayed Contact Sensitization Response to Croton Oil, presented at the American College of Toxicology in Washington, DC, November, 1985.

61. Gad, S.C. Interpretation and Utilization of Dermal Sensitization Data, presented at the Toxicology Roundtable, October, 1985.

62. Gad, SC. *In Vitro* Models in Teratology, presented at the Toxicology Roundtable Oct 1985.

63. Gad, S.C., Dobbs, D.W., Dunn, D.J., Gunsen, D., Reilly, C., and Walsh, R.D. Elucidation of the Delayed Contact Sensitization Response to Croton Oil, presented at the 1985 American College of Toxicology Meetings, Washington, DC, November, 1985.

64. Rinehart, W.E., and Gad, S.C. Current Concepts in Occupational Health: Metals-Chromium, presented at the IHF 50th Anniversary Symposium, Pittsburgh, PA, November, 1985.

65. Gad, S.C. Industrial Approaches to Screening for Neurotoxins, presented by invitation at EPA Neurotoxicity Division, Research Triangle Park, NC.

66. Gad, S.C. Toxicology as Prerequisite in Hazard Communication, presented at the IHF Occupational Physicians Course, December, 1985.

67. Gad, S.C. Carcinogenesis, Teratogenesis and Reproductive Hazards, presented at IHF Occupational Physicians Course, December, 1985.

68. Czerniecki, B., Gad, S.C., Reilly, C., Smith, A.C., and Weitz, G. Phorbol Diacetate Modulates Oxy Radical Production and Tumor Production by Mezerein, presented at the 1986 Cancer Research Meeting.

69. Gad, S.C., Darr, R.W., Dobbs, D.W., Dunn, D.J., Reilly, C., and Walsh, R.D. Evaluation

of Additional Test Materials and Design Variables in (and Odd Technical Notes From) the Mouse Ear Swelling Test (MEST), presented at SOT Meetings, March, 1986.

70. Gad, S.C., Darr, R.W., Dobbs, D.W., Dunn, B.J., Reilly, C., and Walsh, R.D. Comparison of the Potency of 52 Dermal Sensitizers in the Mouse Ear Swelling Test (MEST), presented at SOT Meetings, March, 1986.

71. Gad, S.C., Auletta, S.S., Dunn, B.J., Hile, R.A., Reilly, C., Reagan, E., and Yenser, B. A Double Blind Intralaboratory Validation of the Mouse Ear Swelling Test (MEST), presented at SOT Meetings, March, 1986.

72. Powers, W.J., Gad, S.C., Dunn, B.J., Hoffman, G.M., Siino, K.M., and Walsh, R.D. Acute Toxicity of Four Chromates, presented at SOT Meetings, March, 1986.

73. Gad, S.C., Dunn, D.J., Gavingan, F.A., and Peckham, J.C. Acute and Neurotoxicity of 5,7,11-Dodecatriyn-1-o1 (Compound A) and 5,7,11,13-Octadecatetrayne-1,13-Diol (Compound B), presented at the SOT Meetings, March, 1986.

74. Gad, S.C., Rusch, G.M. Reigle, K.S., Peckham, J.C., Hoffman, G., and Darr, R.W. Subacute and Subchronic Inhalation Toxicity of Chlorotrifluoroethylene (CTFE), presented at SOT Meetings, March, 1986.

75. Gad, S.C. The Technical Interview, Your Technical Knowledge, Your Experience and Education - Can You Do the Job: Job Application, Resource and Interview Seminar, presented at SOT Meeting, March, 1986.

76. Gad, S.C. Fundamentals of Toxicology, presented to American Association of Clinical Chemists, April 8 and 10, 1986.

77. Gad, S.C., Dobbs, D.W., Dunn, B.J., Reilly, C., and Walsh, R.W. An Approach to Development Validation and Acceptance of a New Test System in Toxicology - The MEST, presented at the Johns Hopkins Alternative Methods in Toxicology Symposium, April, 1986.

78. Frazier, J., Gad, S.C., and McCulley, J. An Evaluation of Alternatives to the Draize Eye Test: Special One Day Workshop, presented at Johns Hospkins, April, 1986.

79. McCaulley, J., Gad, S.C., and Frazier, J. Comparative Forms and Objectives of Draize Eye Test, presented at American Academy of Ophthalmology.

80. Czerniecki, B., Witz, G., Reilly, C., and Gad, S.C. Tumor Promoters Suppress and Development of Delayed Hypersensitivity in Mouse Skin, presented at the Joint ASPET/SOT Meetings, August, 1986.

81. Gad, S.C. Risk Assessment of Acrylontrile, presented at Second Workshop on Pragmatics of Risk Assessment, Bethesda, MD, October. 1986.

82. Gad, S.C. Toxicology as a Technical Career, a workshop for the 1986 American College of Toxicology Meeting, Philadelphia, PA, November, 1986.

83. Gad, S.C. An Industrial Perspective on a Quantitative Estimation of Risk Associated with Low Level Exposures of Humans - with Acrylonitrile as a Case Study presented at the Midwest Regional Society of Toxicology Meeting, Chicago, November, 1986.

84. Gad, S.C. Scheme for the Ranking and Prediction of Relative Potencies of Dermal

Sensitizers, Based on Data from Several Test Systems, presented at the Society of Toxicology Meetings, Washington, February, 1987.

85. Gad, S.C. Design, Development and Validation of An Alternative Test System: The Mouse Ear Swelling as a Case Study, presented at the Society of Toxicology Meeting, Washington, February, 1987.

86. Gad, S.C. An Approach for the Statistical Analysis of Screening Data in Toxicology, presented at the Society of Toxicology Meeting, Washington, February, 1987.

87. Gad, S.C. The Interview Process - What Works and What Doesn't. Talk for 1987 SOT Placement Committee Workshop, February, 1987.

88. Gad, S.C. Practical Problems in the Use of Alternatives in Research and Testing, at APh.A Meeting, March, 1987 in Chicago,

89. Witz, G., Czerniecki, B., Gad, S.C. and Goldstein, B.D. In Vivo Stimulation of Oxy Radicals by Mouse Skin Tumor Promotors, presented at 2nd International Conference on Anticarcinogensis and Radiation Protection, Gaithersburg, MD, March, 1987.

90. Gad, S.C. IV Procedures in Canines and Other Species; Prospectives, Problems and Alternatives, presented at "The Canine as a Biomedical Model II", July 13-14, 1987 in Kalamazoo, Michigan.

91. Noveroske, J.W., Gad, S.C., Willoughby, C.R., Enticott, J., Wilby, O.K., Tesh, S.A., McAnulty, P.A. and Tesh, J.M. "Study-Dependent Reproductive Differences to a Contragestational Agent"., presented at the European Teratology Society Meetings, September, 1987.

92. Gad, S.C. Initial Assessment of Toxicity Data for the Industrial Hygienist, presented at the Chicago section of the American Industrial Hygiene Association, September, 1987.

93. Gad, S.C. Screening and Data Analysis for Neural and Behavioral Toxicity, presented as a seminar at Monsanto's Environmental Health Laboratories, September, 1987.

94. Gad, S.C. Regulatory Requirements for Safety Testing - A Workshop at Animal Research and Testing: Humane Frontiers. New York City, October 8, 1987

95. Gad, S.C. Screening in Neurotoxicology: Objectives, Design and Analysis, with the Functional Observational Battery as a Case Example presented at the American College of Toxicology, Baltimore, December 1987.

96. Gad, S.C. Screens and Graphical Methods of Analysis in Toxicology, presented at the Society of Toxicology Meetings, Dallas, TX, February, 1988.

97. Andress, J.M., Chengelis, C.P., Gad, S.C., Port, C.D. and Tegtmeyer, M.S. Nephrotoxicity of D- and L-Arginine in Rats, presented at the Society of Toxicology Meeting, Dallas, TX, February, 1988.

98. Rayboum, M.S., DiBartolomeis, M.J., Whorton, M.D., Coyne, R. and Gad, S.C. Biological Risk Assessment for Occupational Exposure to Airborne Particulate During Pharmaceutical Manufacturing Process, to be presented at the American Industrial Hygiene Conference.

99. Gad, S.C. Principles of Screening in Toxicology, presented at Screening for

Neurotoxicology, Research Triangle Park, April, 1988.

100. Gad, S.C. Data Evaluation and Statistical Analysis in Neurotoxicology Screening, presented at Screening for Neurotoxicity, Research Triangle Park, April, 1988.

101. Chengelis, C., Gad, S.C., Levin, S., Semler, D., and Burton, E. Chronic Toxicity of Bemitradine: Gavage vs. Dietary Admix, presented at the PMA Drug Safety West Meeting, Philadelphia, PA, May, 1988.

102. Gad, S.C. Acute and Chronic Toxicity of Chromium. Association of Government Toxicologist Meeting, Bethesda, MD, May, 1988.

103. Gad, S.C. Species Extrapolation, Toxicology Roundtable, Winter Haven, PA, October, 1988.

104. Gad. S.C. Use of Animals in Research, Toxicology Roundtable, Winter Haven, PA, October, 1988.

105. Chengelis, C.P., Gad, S.C. and Levin, S. The Chronic Toxicity of Bemitradine, presented at the American College of Toxicology Meeting, Baltimore, MD, October, 1988.

106. Gad, S.C. Statistics for Toxicologists, presented at the American College of Toxicology Meeting, Baltimore, MD, October, 1988.

107. MacKenzie, K.M., Boynton, B., Hall, R., Field, W., Gad, S.C. and Cook, C. Subchronic Toxicity and Pharmacokinetics of Spironolactone in Rats and Mice, presented at the Society of Toxicology Meeting, Atlanta, GA, February, 1989.

108. Chengelis, C.P., Gad, S.C., Levin, S. and Burton, E. Bemitradine Induced Cardiotoxicity in Rats, presented at the Society of Toxicology Meeting, Atlanta, GA, February, 1989.

109. Haggerty G. C., Morton, S., Rubn, Z. and Gad, S.C. Neurotoxic Potential of Tricresyl Phosphate In Sprague-Dawley Rats, presented at the Society of Toxicology Meeting, Atlanta, GA February, 1989.

110. Gad, S.C. Recent Developments in Reducing, Refining and Replacing Animal Use in Toxicologic Research and Testing, presented at the Society of Toxicology Meeting, Atlanta, GA, February, 1989.

111. Gad, S.C., Semler, D.E., Denault, S. and Levin, S. Toxicology of SC-48334, A Potential Anti-HIV Drug, presented at the Technical Community of Monsanto, St. Louis, Mo, April, 1989.

112. Coyne, R.S., Gad, S.C. and Chengelis, C.P. Health Hazard Assessment and Management in Research and Manufacturing Facilities for the Pharmaceutical Industry, presented at the American Industrial Hygiene Conference Meeting, St. Louis, Mo, May, 1989.

113. Oshiro, Y., Piper, C.E., Gad. S.C., Rohrbacher, E., Balwierz, P.S., Soelter, S.G., Witz, G. and Goldstein, B.D. Genotoxic Activities of Mucondialdehyde, presented at the Fifth International Conference on Environmental Mutagens, Cleveland, OH, July, 1989.

114. Gad, S.C. Segment II Studies: An Approach to Analysis, presented at the Teratology Society Meeting, Richmond, VA, June, 1989.

115. Costello, A., Gad, S.C., and Chengelis, C.P.: Validation Study for a Guinea Pig Host Resistance Assay, presented at the ASPET meeting, Salt Lake City, UT, August, 1989.

116. Gad, S.C. Predictive Value of Animal Safety Data for Results in Humans, presented at the Toxicology Round Table, Lake Geneva, WI., September 1989.

117. Gad, S.C. Rodent Carcinogenicity Study Design and Interpretation: Industry Experience, presented at the Toxicology Round Table, Lake Geneva, WI., September, 1989.

119. Morton, S.R., Haggerty, G.C. and Gad, S.C. Pharmacological Validation of a Neurobehavioral Test Battery in Sprague Dawley (SD) Rats, presented at the Society of Neuroscience meeting, Phoenix, AZ. October, 1989.

120. Gad, S.C. Model Selection in Toxicology: Principles and Practices, presented at the American College of Toxicology, Williamsburg, October, 1989.

121. Gad, S.C. Acute Toxicity Data: Uses, Requirements and Scope, presented at the American College of Toxicology, Williamsburg, October, 1989.

122. Gad, S.C. Neurotoxicity Testing of Pharmaceuticals - Tiered vs. Data Directed Approach, presented at the PMA Drug Safety West meeting at Indianapolis, in November 1989.

123. Naumann, D.B., Conine, D.L., Hecker, L.H. Sargent, E.V., Gad, S.C., Herning, J.S., Brooks, L., Koening, G.R., Shah, P.V., Boehlert, J.P. and White T.X.: Application of the PMA Procedure for Setting Residue Limits to Methylene Chloride, presented at the Society of Toxicology meeting at Miami in February, 1990.

124. Conine, D.L., Galer, D.M., Sprague, G.L., Hecker, L.H., Neaumann, B.D., Brooks, L., Sussman, R.G., Sargent, E.V., Gad, S.C., Mehring, J.S., Boehlert, J.P. and White, T.X.: Procedures for Setting Health-Based Residue Limits for Organic Volatile Impurities in Pharmaceuticals, presented at the Society of Toxicology Meeting at Miami in Feb., 1990.

125. Haggerty, G.C., Morton, S., Levin, S., Ruben, Z. and Gad, S.C.: Neurotoxic Profile Induced by Subchronic Exposure to Trimethyltin in Sprague Dawley (SD) Rats, presented at the Society of Toxicology meeting at Miami, FL , February, 1990.

126. Guzzie, P.J., Oshiro, Y., Soelter, S.G., Balwierz, P.S., Piper, C.E., Gad, S.C. and Young, R.R.: Genotoxic Activity of Adenosine and an Adenosine-Analog Drug, presented at the Environmental Mutagen Society meeting, Albuquerque, N.M., March, 1990.

127. Oshiro, Y., Gad, S.C., Semler, D.E., Miller, G.K,. Chengelis, C.P, Levin, S. Guzzie, P.J. Preclinical Toxicology Studies of an Anti-AID's Drug, presented at he 15th International Cancer Congress, Hamburg, August, 1990.

128. Chengelis, C.P., Gad, S.C., Frank, P., Cornell, S., and Brouseau, P. Lack of Immunotoxicity associated With Lomefloxacin, a Quinoline Anti-Bacterial, presented at the `1990 Society of Toxicology meeting.

129. Gad, SC. Preclinical Safety Evaluation Methods: A Survey of Animal and Alternative Tests, presented at the Dermal Clinical Evaluation Society, Arlington, Virginia, September, 1990.

130. Gad. S.C. Methods for Predicting Relative Potency of Sensitizers, presented at the 1990 Mechanisms of Immunotoxicity meeting in Williamsburg, VA.

131. Gad, S.C. <u>In Vitro</u> Developmental Toxicity: Theory, Uses and Standards, presented a the 1990 American College of Toxicology Meeting, October, in Orlando, FL.

132. Chengelis, C.P., Gad, S.C., Levin, S. and Costello, A. The Role of Epinephrine in Bemitradine Related Adrenal and Cardiac Damage, presented at the 1990 American College of Toxicology Meeting, October, in Orlando, FL.

133. Haggerty, G.C., Morton, S., Levin, S. and Gad, SC. Evaluation of Two Alkyltin Compounds in the Rat, presented at the 1991 Society of Toxicology Meeting, March, in Dallas.

134. Gad, S.C., Burton, E., Chengelis, C.P., Levin, S., Piper, C.E., Oshiro, Y., and Semler, D.E. Mechanism Studies of the Nongenotoxic Carcinogen Bemitradine (SC-33643), presented at the 1991 Society of Toxicology Meeting, March, in Dallas.

135. Gad, S.C. Impact of Recent Pending Legislation Affecting the Use of Animals in Research on Research and Development, presented at the 1991 Society of Toxicology Meeting, March, in Dallas.

136. Gad, S.C., Acute and Short Term Toxicity Testing, presented at the World Health Organization Training Seminar on Risk Assessment, Ottawa, May, 1991.

137. Gad, S.C., In Vitro Assays for Acute Studies, presented at the World Health Organization Training Seminar on Risk Assessment, Ottawa, May, 1991.

138. Gad, S.C., Information Sources in Dermal Toxicology, presented at the DCES meeting, Washington, D.C., June, 1991.

139. Gad, S.C., Safety Assessment for Drugs, Center for Professional Advancement, New Brunswick, N.J., August, 1991.

140. Gad, S.C., Routes in Toxicology, presented at the ACT Meeting in Savannah, Georgia, October, 1991.

141. Gad, S.C., Intranasal Administration, presented at the ACT Meeting in Savannah, Georgia, October, 1991.

142. Gad, S.C., Alternatives to In Vivo Eye Irritation, presented at the Aberdeen conference on In Vitro Alternatives for Toxicology Testing, February, 1992.

143. Galer, D.M., Curren, R., Gad, S.C., Gautheron, P., Leong, B., Miller, K., Sargent, E., Shah, P.V., Sina, J., and Sussman, R.G., An 11-Company Collaborative Evaluation of Alternatives to the Eye Irritation Test Using Chemical Intermediates, presented at the Johns Hopkins CAAT Conference, April, 1992.

144. PMA/Drusafe In Vitro Toxicology Task Force. A Collaborative Evaluation of An In Vitro Muscle Irritation Assay, presented at the SOT meeting in New Orleans, Louisiana, March, 1993.

145. Gad, S.C., Preclinical Safety Assessment of Pharmaceuticals in Animals; Overall Performance and a Historical Review of Failures, presented at the American College of Toxicology Mtg, New Orleans, October, 1993.

146. Gad, S.C., Mouse Ear Swelling Assay, presented at the American College of Toxicology Mtg, New Orleans, October, 1993.

147. Gad, S.C., The Mouse Ear Swelling Test, presented at the 2nd Summer School on Immunotoxicology, Beaune, France, October, 1993.

148. Haddad, S., Gad, S.C., Tardif, R., and Krishnan, K., Statistical Approaches for the Validation of Physiologically-Based Pharmacokinetic (PBPK) Models, presented at the SOT meeting in Baltimore, March, 1995

149. Gad, S.C., Smoke Toxicity "Standard" Test Method for Materials, presented and panel chaired at the International Colloquium on Advances in Combustion Toxicology, Oklahoma City, April, 1995

150. Gad, S.C., New Research Avenues in Combustion Toxicology, presented and panel chaired at the International Colloquium on Advances in Combustion Toxicology, Oklahoma City, April, 1995

151. Gad, S.C. Histologic and Clinical pathology in the Safety Assessment and Development of New Therapeutic Agents, at International Laboratory Animal Science Congress, Helsinki, Finland, July, 1995

152. Gad, S.C. Preclinical Toxicity Testing in the Development of New Therapeutic Agents, At International Laboratory Animal Science Congress, Helsinki, Finland, July, 1995

153. Gad, S.C. IRAG Organotypic Models for the Assessment/Prediction of Ocular Irritation, presented at the American College of Toxicology, November, 1995, Vienna, Virginia

154. Gad, S.C. Sole Proprietorship Consulting in Toxicology, presented at the American College of Toxicology, November, 1996, Valley Forge, PA.

155. Gad, S.C. Toxicokinetics in the Safety Assessment of Medical Devices, presented at the American College of Toxicology, November, 1996, Valley Forge, PA.

156. Gad, S.C. Statistical Analysis and Experimental Design for Carcinogenicity Bioassays, presented at the American College of Toxicology, November, 1997, McLean, VA.

157. Gad, S.C. General Principles in the Design and Conduct of Large Animal Toxicology Studies, presented at the American College of Toxicology, November, 1998, Orlando, FL

158. Gad, S.C. PD/PK Data in the Prediction and Avoidance of Serious Adverse Events in Patient Populations, presented at "Pharmacokinetic/Pharmacodynamic Drug Development," March 26, 1999, Arlington, VA.

159. Gad, S.C. Acute Toxicology Testing: History, Perspectives and Current Practices, presented at "Toxicology for the Next Millennium", NY Academy of Sciences, September 22, 1999, Warrenton, VA.

159. Gad, S.C. Are Unsafe Drugs Entering the Marketplace Too Easily and Remaining Too Long? at American College of Toxicology meeting, November 9, 1999, McClean, Va..

160. Gad, S.C. AOO (any other Orifice) Toxicology, at Toxicology Roundtable, Absecon, NJ, October 17, 2001

161. Gad, S.C. Issues and Alternative Models for Sensitization Testing at Toxicology Roundtable, Absecon, NJ, October 17, 2001

162. Gad, S.C., Gad, S.D. and Gad, S.E., A Functional Observational Battery (FOB) for use in Dog Toxicity Studies: Development and Validation, presented at the Society of Toxicology, Nashville, TN., March, 2002

163. De, M., Martel, E., Gad, S.C. and Shadiack, A., PT-141: Evaluation of Effects on Respiration in Unrestricted Conscious Rats Following Single Intravenous Administration, to be presented at the Safety Pharmacology Society, Philadelphia, PA, September, 2002

164. De, M., Gad, S.C. and Shadiack, A. A Comparison of the Effects of PT-141 and Apomorphine on Behavioral and Physiological State Assessed by the Irwin test and Body Temperature in Rats, to be presented at the Safety Pharmacology Society, Philadelphia, PA, September, 2002

165. Gad, S.C. Challenges in Forensic Toxicology: From Criminal Arsenic Poisoning to was he drunk before he drowned?, to be presented at the Mid-Atlantic Society of Toxicology meeting, October 8, 2002.

166. Gad, S.C. Drug Safety Issues in Aerosol Therapy, to be presented as part of Clinical and Business Developments in Aerosol Therapy, Institute for International Research, Boston, MA., 21 Oct, 2002

167. Gad, S.C. The Great Debate: Are Dietary Supplements Safe as Currently Regulated?, to be presented at the American College of Toxicology Meeting, Hershey, PA., 12 November, 2002.

168. Gad, S.C. Active Drug Metabolites in Safety Pharmacology Evaluation, presented at the MDS Pharma Safety Pharmacology Meeting, Lyon, France, December 5, 2002.

169. Gad, S.C., Effective and Efficient Melding of Biocompatabilty and Drug Safety Evaluation Requirements, Combination Product Conference, Barnett, Washington, D.C., July 31, 2003

170. Gad, S.C. Capturing, Avoiding, and Solving Pre-Clinical Challenges, Combination Product Conference, Washington, D.C., July 31, 2003

171. Gad, S.C., The Great Debate: Are Statins Safe as Currently Prescribed – An Introduction, American College of Toxicology, Washington, D.C., November 4, 2003.

172. Gad, S.C. "Drug-Drug Pharmacokinetic/Toxicokinetic Interactions", Combination Drugs and Drug-Drug Interactions Conference, Philadelphia, PA, November 18, 2003.

173. Gad, S.C. "Nonclinical Efficacy and Safety Assessment for Pharmaceutical Combination Products", Combination Drugs and Drug-Drug Interactions Conference, Philadelphia, PA, November 18, 2003.

174. Gad, S.C.; Data, Mechanisms and Sounds Science: The basis for Evaluating Causation and Resolving Workman's Compensation and Forensic Toxicology Cases, McAngus Goudelock & Courie Annual Conference, Charlotte, NC, November 20, 2003.